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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,368	06/28/2001	David M. Allen	P1067	2222

7590 02/27/2004

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,368	ALLEN, DAVID M.	
	Examiner	Art Unit	
	JOHN D PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-10 and 12-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18-32 and 38-41* is/are allowed.

6)☒ Claim(s) *1-3,8,10,12-14,16,33,34,36 and 42* is/are rejected.

7)☒ Claim(s) *3,9,15,17,35 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-3, 8-10, 12-42 are pending.

Claim 3 stands objected to under 37 CFR 1.75(c) for the reasons of record, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Applicant's arguments have been considered but found unpersuasive. There does not appear to be a specialized definition in the originally filed disclosure that "penetration into said sub-dermal tissue" has an effect that is beyond the effect obtained when the composition has been injected into the same subdermal tissue. Claim 3 is inconsistent with claim 1 because the injection *into* the subdermal soft tissue in claim 3 means that mobilizing agent of claim 1 is not "in an amount sufficient to enable said macrolide antibiotic to penetrate into said sub-dermal tissue." The injection has enabled the same effect, not the mobilizing agent. Applicant is invited to adopt a claim language that overcomes this problem. The new claim language should of course find adequate descriptive support from the originally filed disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 42 lacks antecedent basis for "said organogel compound."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 10, 12, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Chemical Abstracts 132:69251.

Chemical Abstracts 132:69251 explicitly discloses a composition that is a mixture of erythromycin and benzyl alcohol + acetone + isopropanol (TPDS) that is topically administered to treat acne vulgaris. It is disclosed that in acne vulgaris, "infiltration of the antibiotics into the infected s.c. layers is highly desirable." The erythromycin mixture was transported across the epidermal barrier. Erythromycin was detected in the underlying muscles and various organs.

The Examiner takes note of the fact that "s.c. layers," is subcutaneous layers, and subcutaneous is synonymous with subdermal. See for example Stedman's Medical Dictionary, page 1692 (see entries for "subdermic" and "subcutaneous"). Stedman's is mentioned merely for the purpose of noting that the Examiner's interpretation of the cited reference is proper.

Therefore, the cited reference discloses that acne vulgaris manifests infected subdermal layers, and as a result, acne vulgaris satisfies applicant's claim language, "a disease state resulting from a microbial infection affecting sub-dermal soft tissue." The cited reference discloses topically delivering erythromycin to alleviate acne vulgaris. The cited reference also discloses penetration of erythromycin into the subdermal region. The penetrating TPDS solvent mixture contains three ingredients, and each of those ingredients can be considered a mobilizing agent or penetrating enhancing adjuvant. For these reasons, the cited reference anticipates the claimed invention.

Claims 10, 12, 13, 16, 33, 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Oh et al.

Oh et al. explicitly disclose a liposomal formulation of azithromycin (see p. 2105, the section, "Preparation of azithromycin-loaded liposomes"). Liposomal formulation + the surfactant Triton X-100 is also disclosed (*id.*). Intracellular uptake is disclosed (p. 2104, paragraph bridging the left and right columns).

Applicant's claim language is readable on Oh's azithromycin-loaded liposome formulation. While Oh et al. do not specifically describe using the liposomal formulation for treating disease state resulting from a microbial infection affecting sub-dermal soft tissue, all of the rejected claims are directed to the composition per se, and the language of the rejected composition claims is readable on Oh's liposomal formulation.

Given that applicant's specification discloses that the preferred PLO gel is liposome based (p. 5, lines 13-14), and that present invention encompasses injectable formulations (i.e. not just gels, see e.g., claim 3), there is no question that Oh's azithromycin-loaded liposomal formulation would necessarily possess the functions and properties claimed by applicant. Further, it is the Examiner's position that Triton X-100 meets the claimed "penetration enhancing adjuvant" feature. Triton X-100 is a well-known substance having good surface active properties. Such a surface active substance would meet the "penetration enhancing adjuvant" feature because penetration is affected by surface active properties.

Applicant is requested to review MPEP 2112 and 2112.02 in responding to this ground of rejection and any other ground of rejection where the Examiner relies on inherency or properties that are necessarily possessed (but not explicitly disclosed) by the prior art. It is well settled in patent law that "if the composition is physically the same, it must have the same properties." MPEP 2112.01. A prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. Schering Corp. v. Geneva Pharmaceuticals Inc., 67 USPQ2d 1664, 1667 (Fed. Cir. 2003). The court in Schering expressly rejected a contention that inherent anticipation requires recognition in the prior art. Id. In sum, the claims are anticipated here because

the cited reference discloses a composition that contains ingredients, which would necessarily possess the properties now claimed by applicant.

Claims 1-2, 8, 10, 12, 14 stand rejected under 35 U.S.C. 102(b) as being anticipated by Chemical Abstracts 100:73895 for the reasons of record. See pages 3-4 of the previous Office Action (mail date: 7/15/03).

Applicant's arguments relative hereto have been given due consideration but they were deemed unpersuasive. Applicant disagrees with the Examiner's statement that acne meets applicant's claim language, "disease state resulting from a microbial infection affecting sub-dermal soft tissue." However, it has already been established earlier in this Office Action in the discussion of Chemical Abstracts 132:69251 that acne does in fact meet the requirements of applicant's claim language. Note, the latter Chemical Abstracts is mentioned here merely to show that the Examiner's interpretation of the cited reference here is accurate. Applicant's argument regarding acne is therefore erroneous.

Applicant also argues that the feature of mobilizing agent (to enable erythromycin to penetrate into the subdermal tissue) is not disclosed by the cited reference. This is a most erroneous argument. The cited reference here discloses erythromycin in an ointment base containing hydrogel of methyl cellulose with Tween 80, cetylstearyl alcohol and triethanolamine. Applicant's own specification discloses that organic

hydrogels are preferred and methylcellulose gel are suitable mobilizing agents (p. 6, lines 15-24). Applicant can't have it both ways. If hydrogels and methylcellulose gels are suitable as mobilizing agents in applicant's composition, it is erroneous to argue that prior art composition that contains the same methylcellulose hydrogel cannot serve that function. Hence, the cited reference clearly discloses the same mobilizing agent as applicant's claims.

Regarding Tween 80, cetylstearyl alcohol and triethanolamine, applicant is mistaken in arguing that the Examiner designated them as mobilizing agents. Rather, the Examiner stated that any one of them "would serve the function of a **penetrating enhancing adjuvant** from their solvating and surface active properties" (emphases added; see previous Office action, mail date 7/15/03, p. 4, lines 1-2). Additionally, it must be noted that the specification discloses a variety of solvents as suitable penetrating enhancing adjuvants. Various terpenes and the common organic solvent DMSO are disclosed (p. 7, last paragraph). Clearly, from such a disclosure, the Examiner has sufficient basis for determining the solvent and surface active functioning substances such as Tween 80, cetylstearyl alcohol and triethanolamine as meeting the claimed feature of penetrating enhancing adjuvant.

Claims 10, 12-14, 33, 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kornman (WO 95/09601).

Kornman explicitly discloses a gel composition that contains azithromycin, glycerol monooleate, and hydroxypropyl methylcellulose (p. 9, Example 1).

Kornman's gel would necessarily function as claimed by applicant. Applicant's specification discloses methylcellulose gel and "other organic gels" as suitable mobilizing agents (p. 6, lines 15-24). Clearly, the hydroxypropyl methylcellulose containing gel by Kornman et al. is within the metes and bounds of applicant's mobilizing agent feature. The claims are thereby anticipated.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Chemical Abstracts 85:87225.

Chemical Abstracts 85:87225 explicitly discloses intramuscular injection of erythromycin ethyl succinate to rabbits that have skin syphilomas. Treponema pallidum count decreased by greater than 300 fold upon multiple intramuscular injection of erythromycin.

Skin syphiloma is otherwise known as gumma. Gumma is defined as a chronic focal area of inflammatory destruction in tertiary syphilis thought to be due to localization of Treponema pallidum. Occurrences are found in any organ or tissue. See Dorland's Illustrated Medical Dictionary, 30th edition, 2003, pages 803 and 1840.

The Examiner's position is as follows. First, skin syphiloma meets the claim language, "disease state resulting from a microbial infection affecting sub-dermal soft

tissue in a predetermined area of the body." The fact that skin syphiloma is a chronic **focal** area of inflammatory destruction in tertiary syphilis means that the syphilis infection is already "affecting" other areas of the body, including the subdermal soft tissues. The localization of the Treponema pallidum bacterium on the skin is evidence that the microbial agent is affecting the entire body. Second, for the intramuscular injection to reduce Treponema pallidum count on skin syphilomas, the erythromycin must penetrate the subdermal soft tissue and reach the focal and non-focal areas of Treponema pallidum infection, including subdermal soft tissue.

In sum, an animal that has skin syphilomas is affected by Treponema pallidum infection, i.e. tertiary syphilis, throughout the body, including any organ or tissue such as subdermal tissues. The cited reference explicitly discloses intramuscular injection of erythromycin. Pharmaceutical carrier is necessarily present in an intramuscular injection, and such carrier meets the mobilizing agent claim feature since the intramuscular injection and subsequent penetration/efficacy of the erythromycin is evidence that the carrier was sufficient to function as the mobilizing agent.

For these reasons all of the claimed features are met and the claims are anticipated.

The ground of rejection under 35 USC 103(a) over Macy et al. (US 5,723,447) is hereby withdrawn. In consideration of applicant's remarks and upon further review, the

following *method* claim feature is seen to be lacking in Macy et al. – Injection into subdermal soft tissue so that the macrolide antibiotic reaches microbial infection therein.

Claims 18-32 and 38-41 are allowed.

Claims 9, 15, 17, 35 and 37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Previous indication of allowability of claim 13 and claims specific to azithromycin must be rescinded due to finding of new prior art, cited and discussed hereinabove. The claims have been difficult to search and compare vis-à-vis teachings of prior art due to the subdermal features, wherein inherency issues have been particularly difficult to analyze. Applicant is invited to telephone the Examiner to expedite the further handling of this application.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620, effective February 3, 2004.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Thurman Page, can be reached on (571)272-0602, effective February 3, 2004.

The fax phone number for the organization where this application or proceeding is assigned is (703)872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

JOHN PAK
PRIMARY EXAMINER
GROUP 1600